
Labeling of human embryonic stem cells with iron oxide nanoparticles and fluorescent dyes for a non-invasive cell depiction with MR imaging and optical imaging

Grant Award Details

Labeling of human embryonic stem cells with iron oxide nanoparticles and fluorescent dyes for a non-invasive cell depiction with MR imaging and optical imaging

Grant Type: SEED Grant

Grant Number: RS1-00381

Investigator:

Name:	Heike Daldrop-Link
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$240,214

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Progress Reports

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View Report

Grant Application Details

Application Title: Labeling of human embryonic stem cells with iron oxide nanoparticles and fluorescent dyes for a non-invasive cell depiction with MR imaging and optical imaging

Public Abstract:

Non-invasive imaging techniques for an in vivo tracking of transplanted stem cells offer real-time insight into the underlying biological processes of new stem cell based therapies, with the aim to depict stem cell migration, homing and engraftment at organ, tissue and cellular levels. We showed in previous experiments, that stem cells can be labeled effectively with contrast agents and that the labeled cells can be tracked non-invasively and repetitively with magnetic resonance imaging (MRI) and Optical imaging (OI). The purpose of this study is to apply and optimize these labeling techniques for a sensitive depiction of human embryonic stem cells (hESC) with OI and MRI. Experimental Design: hESC will be labeled with various contrast agents for MRI and OI, using a variety of labeling techniques, different contrast agent concentrations and different labeling intervals (1h – 24h). The cellular contrast agent uptake will be proven by mass spectrometry (quantifies the iron oxides) and fluorescence microscopy (detects fluorescent dyes). The labeled hESC will undergo imaging studies and extensive studies of their viability and ability to differentiate into specialized cell types. Imaging studies: Decreasing numbers of 1×10^5 – 1×10^2 contrast agent-labeled hESC and non-labeled controls will be evaluated with OI and MRI in order to determine the best contrast agent and labeling technique as well as the minimal detectable cell number with either imaging technique. In addition, samples of hESC will be investigated with OI and MRI at 1 min, 2 min, 5 min, 1h, 2h, 6h, 12h, 24h and 48 h in order to investigate the stability of the label over time. Viability and differentiation assays of the hESC will be performed before and after the labeling procedure in order to prove an unimpaired viability and function of the labeled cells. Image analysis and histopathology: For quantitative analyses, MR signal intensities and mean fluorescence signal intensities of the cell samples and the image background will be measured and compared for significant differences between different groups (labeled cells and non-labeled controls, different contrast agents, labeling techniques, different cell numbers, different time points after labeling) using dedicated statistical tests. These quantitative data will be compared with results from mass spectrometry and histopathology. Significance: The derived data should establish and optimize hESC labeling with contrast agents for a non-invasive depiction of the labeled cells with MR and OI imaging techniques. Our method would be in principle readily applicable for monitoring of hESC -based therapies and direct correlations between the presence and distribution of hESC in the target organ and functional improvements. The results of this study will be the basis for subsequent NIH grant applications.

Statement of Benefit to California:

The ability to depict transplanted stem cells non-invasively with imaging techniques is crucial for monitoring of virtually any stem cell based therapy. A better understanding of the signal behavior of contrast agent labeled hESC on MR images will lead the way to a rational and more effective use of hESC-based therapies in preclinical and clinical applications. Since a large state-supported research program is initiated with the proposition 71, we anticipate a variety of evolving applications for our imaging technique in particular in California. Of note, our cell tracking techniques would not only be applicable to hESC, but also to adult stem cells (after tailoring our labeling protocols to certain stem cell populations), thereby providing a key technique for a non-invasive and repetitive monitoring of stem cell based therapies. It is possible, that we may develop new labeling techniques for hESC, which could be patented and, subsequently, be of financial benefit for the state of California via related royalties and licenses. Potential applications of our imaging technique comprise comparative investigations of the in vivo differentiation properties of embryonic and adult stem cells, investigations of the engraftment potential of various stem cell subtypes or genetically engineered hESCs and assessments of therapy effects on hESC differentiation outcomes. Results should be immediately helpful in preclinical assessments of new hESC-based therapies, in the design of related clinical trials, and later, in the assessment of those hESC-based therapies in clinical practice. We expect, that these numerous potential applications of our imaging technique will attract additional federal and private research funding. This could result in increased research activities and associated investments in California. Since we use clinical applicable contrast agents and MR scanners for the proposed study, our findings should be in principle readily translatable to clinical applications. Following transplantation of iron oxides labeled hESC into target organs, the presence and grade of potential clinical improvement could be correlated with the presence and quantity of hESC at the site of disease. Thus, our imaging technique may help to establish and monitor new hESC-based therapies to cure otherwise chronic, long standing or devastating diseases. This could ultimately result in large scale reductions in health care costs in California.

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